# NEW FINDINGS IN MOOD AND ANXIETY DISORDERS ARE IMPORTANT FOR HEALTH INSURERS

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NO FIELD of medicine has undergone a greater evolution of its knowledge base in the last twenty years than psychiatry. Rapid-fire developments in neurochemistry, functional brain imaging and psychopharmacology have yielded new concepts of diagnosis and treatment that are based on hard data and are being validated scientifically. The psychoanalytic construct of the neuroses which prevailed until the late 1960's has given way to psychobiology as, one by one, many of the old neurotic disorders have been found to have a basis in disturbed neurochemistry and subsequently have yielded to chemically-specific psychopharmacologic treatments. Psychoanalysis itself, once hailed as the queen of psychotherapies, has been relegated to the status of training tool for psychotherapists.

This article will limit its focus to the mood and anxiety disorders for the following reasons: a) these two categories constitute approximately 80% of all psychiatric problems experienced by the general public, b) many disorders subsumed by these categories can now be treated quickly and effectively using a combination of pharmacotherapy and brief supportive/educative psychotherapy, c) fixed-fee diagnostic and treatment packages can now be offered to sufferers of these disorders. The paper will consist of three parts: a summary of scientific developments, how one psychiatric provider has operationalized these developments in a clinical setting and a discussion of the implications for insurers, providers and policyholders.

### **Summary Of Recent Scientific Developments**

#### Epidemiology

The latest nationwide multicenter catchment area study of the epidemiology of psychiatric disorders in the community was published in 1984. Anxiety disorders are the most prevalent among all psychiatric disorders, affecting 8% of the U.S. population. Mood disorders have a point prevalence of 6% and a lifetime incidence of 20% (one of every five people will experience a treatable mood disorder at some time during his/her life). At any given time, 14% of the U.S. population (or

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30 million people) require treatment for a mood or anxiety disorder. Fewer than one-third ever receive the treatment they need. Of the 68% affected who do not come to treatment, 15% will eventually commit suicide. Recent studies show that anxiety disorder patients are just as likely to kill themselves as those having mood disorders. It has been estimated that 17% of lost productivity in the work force is accounted for by these two groups of psychiatric disorders.

# Biological Markers

The role of central nervous system (CNS) neurotransmitters in the electrochemical transmission of the neural impulse was delineated in the 1960's. Early measurements of the first identified transmitter substances - acetylcholine, dopamine, norepinephrine, serotonin and their metabolites - were made in the cerebrospinal fluid of humans in the early 1970's. Relative excesses or deficiencies of the various transmitters were correlated with major mood disorders -mania and depression. Later studies demonstrated central neurotransmitter imbalances in the anxiety disorders as well. It was not long before peripheral measures of central transmitter metabolites were discovered, thus obviating the need for lumbar punctures in order to measure these chemicals. The first reliable peripheral assay was of urinary 3-methoxy-4-hydroxyphenylglycol (MHPG). This is the end metabolite of CNS norepinephrine. Low values were correlated with bipolar I depression, intermediate values with unipolar and bipolar II depression and high values with mania. Later it was discovered that the dexamethasone suppression test (DST), which assessed the functional integrity of the hypothalamic-pituitary-adrenal axis, could be used to confirm certain major depressions. 2 The neurotransmitter responsible for neural conduction along this axis is norepinephrine; deficiency in brain norepinephrine results in non-suppression of cortisol following the administration of oral dexamethasone. Approximately 50% of major depressives demonstrate cortisol nonsuppression when given a DST. Likewise, the thyrotropin-releasing hormone stimulation test (TRHST) shows a blunted response in around 50% of major depressives.<sup>3</sup> This test of the hypothalamic-pituitary-thyroid axis provides an indirect assessment of both serotonin and norepinephrine pathways. The TRHST, when used together with a DST, increases the likelihood of confirming a biological depression, helps distinguish

a norepinephrine-deficient depression from a serotonin-deficient depression and may help discriminate unipolar from bipolar depression. Platelet monoamine oxidase measured in peripheral blood is a direct reflection of central monoamine oxidase (MAO) activity. MAO is a presynaptic enzyme which facilitates the breakdown of brain monoamines (including serotonin). Blockage of the action of MAO by the MAO inhibitor antidepressants causes a synaptic build-up or accumulation of transmitters, thus ameliorating depression. A number of other laboratory marker tests have been evaluated but found wanting in independent validation studies. In the 1980's, a technique was developed to examine binding of chemical substances on the CNS postsynaptic neural terminus. This opened a whole new area of receptor neurochemistry, and helped to explain the long 3 to 4 week latency between the beginning of drug therapy and the onset of a treatment response. Whereas the quantity of neurotransmitter is increased almost immediately after antidepressant drugs are ingested, it takes weeks for receptor sites to increase in number and sensitivity to the neurotransmitters. In addition, post synaptic binding sites for various drug moieties have been discovered. Some drugs can apparently exert direct action on the neural terminus in addition to their indirect effects via the build-up of neurotransmitters.

# Brain Imaging

Research studies utilizing brain scans of patients with various psychiatric disorders have been extensively reported. The literature is replete with studies on depressive, manic and schizophrenic patient populations utilizing the following technologies: CT, MRI, SPECT, PET and QEEG. The most definitive and widely replicated studies are those of schizophrenic populations. These studies confirm that schizophrenics show evidence of a generalized hypofrontality in both structure and function and also an increased ventricle to brain substance ratio. Studies on mood-disordered populations have yielded inconsistent and indeterminate findings. Some studies suggest a transient hypofrontality in depressives which seems to resolve when the patient improves clinically. Ventricular/brain ratios show a transient increase in some depressed patients. The most promising technology for assessing depression appears to be QEEG or quantitative electroencephalography. I have used this technology for twelve years and have established profiles of electrophysiologic abnormalities for various depressive subtypes.<sup>5,6</sup> There is a problem that prevents the widespread acceptance and use of this technology as an aid for psychiatric diagnosis. Because of early commercialization by competing manufacturers of QEEG devices, standardization of data collection

procedures and statistical measuring parameters has failed to evolve. This means that data collected with one device cannot be compared with data collected using the device of another manufacturer. Progress in crosscenter validation has been slow. Credibility of this interesting procedure awaits a much-needed agreement to standardize procedures.

# Psychopharmacology

Much of the impetus for research in neurochemistry and receptor chemistry was the early investigations to illuminate the mechanism of action of the antidepressant and mood stabilizing compounds. New insights into neurochemistry have given rise to a series of new psychopharmacologic compounds which are designed to be highly chemical-specific. New drugs with names like desyrel, prozac, anafranil, wellbutrin, zoloft are unrelated to the older tricyclic antidepressants. Each targets a specific neurotransmitter system without much affecting the others. The hope is that they might offer a faster onset of action with fewer side effects. It is also hoped they will target specific chemical-deficient depressions. Well over 100 neurotransmitters have been discovered. When we develop tests to measure these systems, our knowledge of chemical specificity will multiply accordingly. As one can see, "seat-of-thepants" office-based psychopharmacotherapy of mood and anxiety disorders is now passé. A new cadre of highly trained clinical psychopharmacologists has emerged. Presently about 200 such specialists are in practice throughout the U.S. They function mainly as tertiary consultants, treating patients who have failed to respond to psychotherapy and/or a standard course of tricyclic antidepressants. Their comprehension of neurochemistry allows them to use custom-tailored drug combinations after a definitive subtype diagnosis has been established and bolstered by objective laboratory and neurophysiologic testing. These superspecialists have posted an impressive track record in the successful drug treatment of depressed patients previously considered to be refractory to standard treatments.7,8 At the same time, new concepts in the treatment of anxiety disorders have emerged from the neurochemistry revolution. New drugs like buspar are effective and do not have the addictive potential of the widely prescribed benzodiazepine anxiolytics. The anxiolytic property of both tricyclic and MAO inhibitor antidepressants, has now been recognized. As a result, a massive relearning initiative has been undertaken by the American Psychiatric Association in collaboration with the National Institutes of Mental Health. This joint effort has targeted both the general public and the medical profession and accounts for numerous feature

articles appearing in the lay press and for frequent TV specials.

## New Strategies for Service Delivery

In the late 1970's, as the neurochemical revolution gained momentum in psychiatry, economic trends in health care delivery and insurance realignments in the health sector foretold the era of rapid socialization of medicine that is now upon us. It became clear that psychiatrists must develop new strategies for the delivery of cost-effective and time-efficient services if we were to survive as a viable specialty of medicine. Psychotherapy was too costly, time-consuming and unpredictable in terms of its outcomes. By 1980, it was apparent which psychiatric disorders could be treated effectively and relatively inexpensively - those with a demonstrated biologic basis, namely, the affective or mood disorders and the anxiety disorders.

Our medium-sized community hospital established what was then a pilot program for the biochemically based diagnosis and treatment of mood disorders. Its laboratory established and standardized procedures for performing the DST, TRHST and urinary MHPG. A QEEG device was obtained. Structured interviews for mood and anxiety disorders were developed and automated, as were anxiety and depression rating scales. Assessment protocols were established, standardized and controlled using non-patients for statistical comparison. Outcome studies were designed and carried out on the first 200 patients who underwent assessment and treatment. As we learned more about the uses and limitations of our testing procedures, we became skilled at diagnostic subtyping. We used the objective data to confirm diagnoses and to help with the discrimination of diagnostic subtypes. Once a system of diagnostic subtyping was instituted, we were able to custom-tailor drug treatments to specific chemical and phenomenologic subtypes. This eventuated in more rapid treatment responses, fewer drug side effects, shorter hospital stays (averaging 12.5 days), and fewer treatment failures. These advances were not easily achieved, however. As one can see from Figure 1, a considerable refinement of diagnostic acumen is required. Access to the technology that enables this level of sophistication is also required. Two outcome studies performed on consecutive groups of depressed inpatients (each with an N=100) showed that more than 75% of our patients had a successful treatment outcome by one to three months after treatment was started. The second group was comprised of patients who were considered refractory to previous treatment with psychotherapy\_and/or standard tricyclic antidepressant medications.' Recent refinements in the assessment/treatment process in-

clude the following: the design of a unique setting to house these short-stay patients, which includes a group therapy program aimed at educating the patient about the nature, course and treatment of the illness, while enlisting compliance with the treatment; the development of an adult day treatment center or day hospital program to support patients without adequate psychosocial support systems in the community; development of an automated expert system to guide a clinician through the assessment, analyze the patient's clinical, laboratory, QEEG and historical data, produce a definitive subtype diagnosis and generate a treatment plan. The software system also helps with side effects, adverse drug interactions, treatment failure, etc. The assessment has now been operationalized as an outpatient diagnostic center. This allowed us to utilize inpatient days for chemical stabilization only, reducing the inpatient stay to 7 to 10 days except when electrocortical therapy (ECT or shock treatment) is required.

#### Discussion

Major health insurers are "sitting in the catbird seat" in terms of shaping the policies and behaviors of health care providers. This applies to individuals (physicians, allied health professionals, ancillary service providers) and to institutions (hospitals, nursing homes, equipment companies, home health agencies, etc). Doctors, hospitals and other providers gravitate toward those procedures that are compensated, and abandon or avoid those that are less well compensated or no longer compensated. The financial "reward-punishment paradigm" is an effective behavior modifier. The challenge, of course, is to get into the proactive mode and use this power in the best interests of everyone involved - the insurer, the service provider and the patient/policyholder.

In the past, many insurers covered inpatient psychiatry on the same basis as other medical services, while outpatient services had stricter limits and higher co-payments were required. Psychiatric treatments tended to be long-term and expensive. It was more difficult to assess "exposure" for psychiatric conditions. Recently, lifetime caps were applied to all covered psychiatric services, often ranging from \$10,000 to \$25,000. Another technique to limit "exposure" was to make psychiatric coverage elective at extra cost to the consumer. Most consumers cannot conceive that they would ever need such coverage, so they don't elect it. Unfortunately for them, they do not have access to the prevalence figures presented here or to the knowledge that a hereditary biochemical mood or anxiety disorder will strike one out of every five (an average of one per family).

DSYTHYMIC DISORDER ---PRIMARY CYCLOTHYMIC DISORDER SCHIZOPHRENIA
PERSONALITY DISORDERS
BORDERLINE SYNDROME
ANOREXIA/BULEMIA
ALCOHOLISM
DRUG ABUSE
ANXIETY DISORDERS OTHER PSYCHIATRIC ILLNESSES MINOR DEPRESSION DIAGNOSTIC SCHEMA OF MOOD DISORDERS MI COPD CORONARY BYPASS REMAL DIALYSIS METABOLIC/ENDOCRINE INFECTIONS MEDICAL ILLNESS MEDICATIONS
BARBITURATE
BEAR BLOCKERS
BEACODIAZEPINES
CARDIAC GLYCOSIDES
OPIATES
STEROIDS
TAGAMET
L'EOPA
ANTIHYPERTENSIVES
OTHER SECONDARY O.B.S.: ALZHEIMERS MULTI-INFARCT OTHER CANCER GRIEF OBJECT LOSS FINANCIAL LOSS JOB LOSS REACTIVE REVERSE VEGETATIVE MAJOR DEPRESSION Figure 1 NONENDOGENOUS ATYPICAL UNIPOLAR NEUROTIC ANXIETY ABULIC REACTIVE RELATED HYSTEROID DYSPHORIA EXCITED DEPRESSED SCHIZOAFFECTIVE PRIMARY BIPOLAR DEPRESSED ENDOGENOUS WITH PSYCHOSIS MIXED WITHOUT
PSYCHOSIS BIPOLAR DISORDER RAPID CYCLING MANIC

It is now possible to assess the exposure for certain psychiatric disorders, i.e. those that are known to be biologically based and, hence, easily and inexpensively treated. Affordable coverage could be designed for those conditions which are treatable by currently available scientific methods. We can offer fixed price diagnostic/treatment packages since our data rests on a firm scientific footing. Nebulous areas of the field — those without a known scientific basis and fad treatments which come and go — do not merit compensation. Figure

2 compares the cost of treating depression by traditional means with the cost of the biopsychiatric approach detailed here. The challenge is to utilize this information, these tools and the rapidly expanding skills of biopsychiatrists to develop streamlined psychiatric coverages which will benefit patients, fairly compensate providers and permit accurate classification by the insurers. This task can be accomplished now if a dialogue between the industry and representative of biopsychiatry can be developed.

Figure 2 Cost Comparison of Traditional vs. Biopsychiatric Treatment of Depression			
	Standard Treatment	<b>Biopsychiatric Treatment</b>	
INPATIENT	30 inpatient days on a psychiatric unit at \$750 per day	Outpatient biopsychiatric assessment followed by 10 inpatient days in a general hospital setting	
	\$22,500	\$6,000	
OUTPATIENT	Weekly psychotherapy and medications monitoring for one year at \$130 per session	Outpatient biopsychiatric Assessment followed by one year of interval medications monitoring	
	\$6,760*	\$2,500*	

<sup>\*</sup> cost of medications not included

### References

- 1. Regier DA, Myers JK, Kramer M. The NIMH epidemiol catchment area program. *Arch Gen Psychiatry* 1984; 41: 934-941.
- 2. Arana GW, Baldessarini RJ, Ornsteen M. The dexamethasone suppression test for diagnosis and prognosis in psychiatry. *Arch Gen Psychiatry* 1985; 42: 1193-1204.
- 3. Loosen PT, Prange AJ. Serum thyrotropin response to thyrotropin-releasing hormone in psychiatric patients: a review. Am J Psychiatry 1982; 139:405-415.
- 4. Lieber AL, Newbury ND. Use of biological markers in a general hospital affective disorders program. *J Clin Psychiatry* 1985; 46:217-221.

- 5. Lieber AL, Prichep LS. Diagnosis and subtyping of depressive disordersbyquantitative electroencephalography: I and II. Hillside J Clin Psychiatry 1988; 10 (1): 71-97.
- 6. Lieber AL, Newbury ND. Diagnosis and subtyping of depressive disorders by quantitative electroencephalography: III and IV. Hillside J Clin Psychiatry 1988: 10 (2): 165-182.
- 7. Lieber AL, Newbury ND. Diagnosis, treatment and outcome in refractory depression. Ann Clin Psychiatry 1991; 3:119-126.
- 8. Guscott R, Grof P. The clinical meaning of refractory depression: a review for the clinician. *Am J Psychiatry* 1991; 148:695-704.